

## Comparative In Vitro Activities of Trovafloxacin (CP-99,219) against 221 Aerobic and 217 Anaerobic Bacteria Isolated from Patients with Intra-Abdominal Infections

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**Four hundred thirty-eight bacteria cultured from specimens of patients with serious intra-abdominal infections were tested by agar dilution against trovafloxacin and other quinolones and antimicrobial agents. Trovafloxacin inhibited 435 strains (99.3%) at  $\leq 2$   $\mu$ g/ml. All the quinolones had similar activities against *Enterobacteriaceae* and *Pseudomonas* sp., but trovafloxacin showed superior activities against streptococci, enterococci, and anaerobic organisms. Because of its excellent in vitro activities against diverse bacteria, trovafloxacin has potential use as a single agent for polymicrobial infections.**

Although currently available quinolone antibiotics have good activity against aerobic gram-negative bacilli, they have limited efficacy against gram-positive and anaerobic bacteria (1a, 3). Because of their limited spectrum of activity, these drugs have not been used as single agents against infections that include both aerobic and anaerobic organisms. Trovafloxacin, a fluoronaphthyridone derivative, is a new antibiotic that is structurally related to other fluoroquinolones but that differs from the older quinolones by having greatly enhanced activities against gram-positive and anaerobic bacteria as well as against gram-negative bacilli (2, 4, 5, 9, 11).

To determine if trovafloxacin would be active as a single agent in mixed infections, we tested the drug against 438 strains of bacteria isolated from 196 patients with intra-abdominal infections. The in vitro activity of trovafloxacin was compared to those of levofloxacin, ciprofloxacin, ofloxacin, and eight other antimicrobial agents frequently used for treatment of intra-abdominal infections.

Aerobic and anaerobic bacteria were cultured from specimens from patients hospitalized for serious intra-abdominal infections, most frequently gangrenous or ruptured appendixes. The bacteria were identified by standard techniques (6, 10) and stored at  $-70^{\circ}\text{C}$  until testing. The species are listed in Table 1.

Antibiotics were provided by their respective manufacturers as follows: trovafloxacin from Pfizer Inc., Groton, Conn.; levofloxacin and ofloxacin from the R. W. Johnson Pharmaceutical Research Institute, Raritan, N.J.; ciprofloxacin from Bayer Inc., West Haven, Conn.; imipenem and ceftioxin from Merck and Co., West Point, Pa.; piperacillin-tazobactam from Wyeth-Ayerst, Philadelphia, Pa.; amoxicillin-clavulanate from Smith-Kline Beecham, Philadelphia, Pa.; cefotetan from Zeneca Pharmaceuticals, Wilmington, Del.; gentamicin from Schering Plough, Kenilworth, N.J.; clindamycin from The Upjohn Company, Kalamazoo, Mich.; and metronidazole from Searle Pharmaceuticals, Skokie, Ill. They were reconstituted according to their manufacturer's instructions, and stock solutions were stored at  $-70^{\circ}\text{C}$ . Piperacillin-tazobactam was tested with a

constant concentration of tazobactam of 4  $\mu$ g/ml. Amoxicillin-clavulanate was prepared in a ratio of 2:1.

An agar dilution method was used for testing all of the strains (7, 8). Organisms were applied to the plates with a Steers replicator that delivered approximately 0.001 ml per spot. Mueller-Hinton agar was used for the facultative and aerobic organisms and was supplemented with 5% whole sheep blood for streptococci. Anaerobes were tested on brucella agar supplemented with vitamin K<sub>1</sub> and 5% sheep blood. Inocula were prepared by growing aerobic organisms in Mueller-Hinton broth at  $35^{\circ}\text{C}$  for 4 h and diluting them to the turbidity of the 0.5 McFarland standard. They were further diluted 1:10 for a final concentration of  $10^4$  CFU/spot. The rapidly growing anaerobes were cultured in supplemented thioglycolate broth overnight at  $35^{\circ}\text{C}$  and diluted to equal the turbidity of the 0.5 McFarland standard. Fastidious anaerobes were suspended in thioglycolate broth directly from the plate. The final inoculum for anaerobes was  $10^5$  CFU/spot.

The plates inoculated with aerobic and facultative organisms were incubated at  $35^{\circ}\text{C}$  in ambient air for 20 h. Plates with anaerobic organisms were incubated in GasPak jars for 48 h. The MIC was defined as the concentration of drug that, after incubation, significantly decreased growth compared to growth obtained on the drug-free growth control plate. The following American Type Culture Collection control strains were tested along with the clinical isolates: *Staphylococcus aureus* ATCC 29212, *Enterococcus faecalis* ATCC 29212, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Bacteroides fragilis* ATCC 25285, and *Bacteroides thetaiotaomicron* ATCC 29741.

There were 438 different strains tested, and 435 were inhibited by  $\leq 2$   $\mu$ g of trovafloxacin per ml (Table 1). Only three strains required more than 2  $\mu$ g of trovafloxacin for inhibition. These were one strain each of *E. coli*, *Staphylococcus haemolyticus*, and a *Fusobacterium* sp.; these strains were highly resistant to the other fluoroquinolones as well. Trovafloxacin, levofloxacin, ofloxacin, and ciprofloxacin had comparable activities against the *Enterobacteriaceae*. Trovafloxacin and ciprofloxacin had similar activities against *P. aeruginosa*. Trovafloxacin was four- to eightfold more active against streptococci and enterococci than the other quinolones. It had activities comparable to those of metronidazole against gram-negative anaerobes and comparable to those of imipenem and amoxi-

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TABLE 1. In vitro activities of trovafloxacin and eleven other antimicrobial agents against 221 aerobic and 217 anaerobic bacteria

Organism (no. of strains) and antibiotic	MIC ( $\mu\text{g/ml}$ ) <sup>a</sup>			% Susceptible <sup>b</sup>
	Range	50%	90%	
<i>E. coli</i> (20)				
Trovaflaxacin	0.06–>32	0.125	0.125	95, 95, 95
Levofloxacin	0.03–>32	0.06	0.06	95, 95
Ofloxacin	0.125–>32	0.06	0.06	95, 95
Ciprofloxacin	0.03–>32	0.06	0.125	95, 95
Imipenem	$\leq 0.125$ –1	$\leq 0.125$	$\leq 0.125$	100, 100
Piperacillin-tazobactam	$\leq 0.5$ –32	$\leq 0.5$	1	95, 100, 100
Amoxicillin-clavulanate	2–4	2	4	100, 100
Cefoxitin	1–4	1	4	100, 100
Cefotetan	$\leq 0.5$	$\leq 0.5$	$\leq 0.5$	100, 100
Gentamicin	$\leq 0.5$	$\leq 0.5$	$\leq 0.5$	100, 100
<i>Klebsiella</i> spp. (20) <sup>c</sup>				
Trovaflaxacin	$\leq 0.015$ –0.06	0.03	0.06	100, 100, 100
Levofloxacin	$\leq 0.15$ –0.06	$\leq 0.015$	$\leq 0.015$	100, 100
Ofloxacin	$\leq 0.015$ –0.125	0.03	0.06	100, 100
Ciprofloxacin	$\leq 0.015$ –0.03	$\leq 0.015$	0.03	100, 100
Imipenem	$\leq 0.125$ –0.25	$\leq 0.125$	$\leq 0.125$	100, 100
Piperacillin-tazobactam	$\leq 0.5$ –64	$\leq 0.5$	$\leq 0.5$	95, 95, 100
Amoxicillin-clavulanate	$\leq 0.5$ –8	4	8	100, 100
Cefoxitin	1–2	2	2	100, 100
Cefotetan	$\leq 0.5$	$\leq 0.5$	$\leq 0.5$	100, 100
Gentamicin	$\leq 0.5$	$\leq 0.5$	$\leq 0.5$	100, 100
<i>Citrobacter</i> spp. (21) <sup>d</sup>				
Trovaflaxacin	$\leq 0.015$ –0.125	$\leq 0.015$	0.03	100, 100, 100
Levofloxacin	$\leq 0.015$ –0.03	$\leq 0.015$	$\leq 0.015$	100, 100
Ofloxacin	$\leq 0.015$ –0.125	0.06	0.06	100, 100
Ciprofloxacin	$\leq 0.015$ –0.06	$\leq 0.015$	$\leq 0.015$	100, 100
Imipenem	$\leq 0.125$ –0.5	$\leq 0.125$	0.5	100, 100
Piperacillin-tazobactam	$\leq 0.5$ –64	$\leq 0.5$	8	90.4, 95.2, 100
Amoxicillin-clavulanate	4–16	8	16	80.9, 100
Cefoxitin	1–64	2	64	80.9, 80.9
Cefotetan	$\leq 0.5$	$\leq 0.5$	$\leq 0.5$	100, 100
Gentamicin	$\leq 0.5$	$\leq 0.5$	$\leq 0.5$	100, 100
<i>Enterobacter</i> spp. (10) <sup>e</sup>				
Trovaflaxacin	$\leq 0.015$ –0.03	$\leq 0.015$	0.03	100, 100, 100
Levofloxacin	$\leq 0.015$ –0.06	$\leq 0.015$	0.06	100, 100
Ofloxacin	$\leq 0.015$ –0.125	$\leq 0.015$	0.125	100, 100
Ciprofloxacin	$\leq 0.015$ –0.03	$\leq 0.015$	0.03	100, 100
Imipenem	$\leq 0.125$ –0.25	$\leq 0.125$	0.25	100, 100
Piperacillin-tazobactam	$\leq 0.5$ –4	2	4	100, 100, 100
Amoxicillin-clavulanate	4–16	8	8	90, 90
Cefoxitin	2–>128	>128	>128	10, 10
Cefotetan	$\leq 0.5$ –32	$\leq 0.5$	4	90, 100
Gentamicin	$\leq 0.5$	$\leq 0.5$	$\leq 0.5$	100, 100
<i>Morganella</i> and <i>Providencia</i> spp. (16) <sup>f</sup>				
Trovaflaxacin	$\leq 0.015$ –0.25	$\leq 0.015$	0.25	100, 100, 100
Levofloxacin	$\leq 0.015$ –1	0.03	1	100, 100
Ofloxacin	$\leq 0.015$ –2	0.06	2	100, 100
Ciprofloxacin	$\leq 0.015$ –0.5	0.03	0.25	100, 100
Imipenem	$\leq 0.125$ –2	1	2	100, 100

Continued

TABLE 1—Continued

Organism (no. of strains) and antibiotic	MIC ( $\mu\text{g/ml}$ ) <sup>a</sup>			% Susceptible <sup>b</sup>
	Range	50%	90%	
Piperacillin-tazobactam	$\leq 0.5$ –>128	2	64	68.8, 75, 93.8
Aoxicillin-clavulanate	1–32	16	32	18.8, 75
Cefoxitin	0.5–16	8	16	68.8, 100
Cefotetan	$\leq 0.5$ –2	$\leq 0.5$	2	100, 100
Gentamicin	$\leq 0.5$ –64	1	16	65.3, 62.5
<i>Proteus</i> spp. (11) <sup>g</sup>				
Trovaflaxacin	0.03–0.125	0.06	0.125	100, 100, 100
Levofloxacin	0.03	0.03	0.03	100, 100
Ofloxacin	0.06	0.06	0.06	100, 100
Ciprofloxacin	$\leq 0.015$ –0.03	$\leq 0.015$	$\leq 0.015$	100, 100
Imipenem	0.25–2	0.25	1	100, 100
Piperacillin-tazobactam	$\leq 0.5$	$\leq 0.5$	$\leq 0.5$	100, 100, 100
Amoxicillin-clavulanate	$\leq 0.5$ –2	$\leq 0.5$	$\leq 0.5$	100, 100
Cefoxitin	1–2	1	2	100, 100
Cefotetan	$\leq 0.5$	$\leq 0.5$	$\leq 0.5$	100, 100
Gentamicin	$\leq 0.5$	$\leq 0.5$	$\leq 0.5$	100, 100
<i>P. aeruginosa</i> (25)				
Trovaflaxacin	$\leq 0.015$ –0.5	0.125	0.25	100, 100, 100
Levofloxacin	0.06–0.5	0.125	0.5	100, 100
Ofloxacin	0.25–2	0.5	2	100, 100
Ciprofloxacin	0.03–0.5	0.125	0.25	100, 100
Imipenem	0.25–2	1	2	100, 100
Piperacillin-tazobactam	$\leq 0.5$ –8	1	4	100, 100
Amoxicillin-clavulanate	32–>128	64	>128	0, 0
Cefoxitin	>128	>128	>128	0, 0
Cefotetan	>128	>128	>128	0, 0
Gentamicin	$\leq 0.5$ –4	1	2	100, 100
<i>Pseudomonas testosteroni</i> / <i>Pseudomonas alcaligenes</i> group (16)				
Trovaflaxacin	$\leq 0.015$ –0.125	$\leq 0.015$	0.06	100, 100, 100
Levofloxacin	$\leq 0.015$ –0.03	$\leq 0.015$	0.03	100, 100
Ofloxacin	$\leq 0.015$ –0.125	$\leq 0.015$	0.125	100, 100
Ciprofloxacin	<0.03–0.5	0.03	0.25	100, 100
Imipenem	$\leq 0.125$	$\leq 0.125$	$\leq 0.125$	100, 100
Piperacillin-tazobactam	$\leq 0.5$ –4	$\leq 0.5$	$\leq 0.5$	100, 100, 100
Amoxicillin-clavulanate	$\leq 0.5$ –1	$\leq 0.5$	1	100, 100
Cefoxitin	$\leq 0.5$ –16	1	2	93.8, 100
Cefotetan	$\leq 0.5$ –2	$\leq 0.5$	$\leq 0.5$	100, 100
Gentamicin	1–2	1	2	100, 100
<i>Enterococcus</i> spp. (29) <sup>h</sup>				
Trovaflaxacin	$\leq 0.015$ –1	0.125	0.5	100, 100, 100
Levofloxacin	0.5–4	1	2	89.7, 100
Ofloxacin	1–8	2	8	37.9, 82.8
Ciprofloxacin	1–16	2	8	20.7, 79.3
Imipenem	$\leq 0.125$ –32	0.5	16	86.2, 86.2
Piperacillin-tazobactam	$\leq 0.5$ –64	8	16	89.6, 89.6, 100
Amoxicillin-clavulanate	$\leq 0.5$ –4	$\leq 0.5$	2	100, 100
Cefoxitin	2–>128	32	>128	34.5, 41.4
Cefotetan	4–>128	>128	>128	3.4, 3.4

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TABLE 1—Continued

Organism (no. of strains) and antibiotic	MIC (µg/ml) <sup>a</sup>			% Susceptible <sup>b</sup>
	Range	50%	90%	
<i>Streptococcus</i> spp. (29) <sup>i</sup>				
Trovafloracin	≤0.015–1	0.03	0.06	100, 100, 100
Levofloxacin	0.25–8	0.5	1	96.6, 96.6
Ofloxacin	0.06–16	1	2	96.6, 96.6
Ciprofloxacin	0.125–16	1	2	65.5, 89.7
Imipenem	≤0.125–2	≤0.125	≤0.125	100, 100
Piperacillin-tazobactam	≤0.5–16	≤0.5	≤0.5	100, 100, 100
Amoxicillin-clavulanate	≤0.5	≤0.5	≤0.5	100, 100
Cefoxitin	≤0.5–16	8	8	96.5, 100
Cefotetan	≤0.5–128	8	8	89.7, 93.1
Clindamycin	≤0.5–128	≤0.5	≤0.5	96.6, 96.6
<i>Staphylococcus</i> spp. (24) <sup>j</sup>				
Trovafloracin	≤0.015–8	≤0.015	0.03	95.8, 95.8, 95.8
Levofloxacin	≤0.015–8	0.06	0.125	95.8, 95.8
Ofloxacin	≤0.015–32	0.25	0.5	95.8, 95.8
Ciprofloxacin	≤0.015–16	0.06	0.125	95.8, 95.8
Imipenem	≤0.125–8	≤0.125	≤0.125	95.8, 100
Piperacillin-tazobactam	≤0.5–32	≤0.5	≤0.5	95.8, 100, 100
Amoxicillin-clavulanate	≤0.5–8	≤0.5	≤0.5	100, 100
Cefoxitin	≤0.5–16	≤0.5	1	95.8, 100
Cefotetan	2–>128	4	16	95.8, 95.8
Gentamicin	≤0.5–4	≤0.5	≤0.5	100, 100
<i>B. fragilis</i> (20)				
Trovafloracin	0.03–0.25	0.06	0.125	100, 100, 100
Levofloxacin	0.25–4	2	2	90, 100
Ofloxacin	1–8	4	4	10, 90
Ciprofloxacin	4–32	16	32	0, 0
Imipenem	≤0.125–1	≤0.125	0.25	100, 100
Piperacillin-tazobactam	≤0.5–>128	1	4	95, 95, 95
Amoxicillin-clavulanate	≤0.5–2	≤0.5	2	100, 100
Cefoxitin	8–64	16	32	80, 95
Cefotetan	8–64	16	32	90, 95
Clindamycin	≤0.5–>128	2	>128	85, 85
Metronidazole	≤0.5–1	≤0.5	1	100, 100
<i>B. thetaiotaomicron</i> (19)				
Trovafloracin	0.06–1	0.125	0.5	100, 100, 100
Levofloxacin	2–32	4	32	10.5, 52.6
Ofloxacin	4–>32	8	>32	0, 15.8
Ciprofloxacin	16–>32	32	>32	0, 0
Imipenem	≤0.125	0.25	1	100, 100
Piperacillin-tazobactam	4–>128	32	64	36.8, 89.4, 94.7
Amoxicillin-clavulanate	≤0.5–2	1	2	100, 100
Cefoxitin	16–64	32	64	15.8, 78.9
Cefotetan	64–>128	128	>128	0, 0
Clindamycin	2–>128	8	>128	10.5, 26.3
Metronidazole	≤0.5–2	1	2	100, 100
<i>Bacteroides ovatus</i> (18)				
Trovafloracin	0.25–1	0.5	1	100, 100, 100
Levofloxacin	2–8	4	8	5.5, 72.2
Ofloxacin	4–16	8	16	0, 11.1
Ciprofloxacin	8–>32	32	>32	0, 0
Imipenem	≤0.125	≤0.125	0.25	100, 100
Piperacillin-tazobactam	2–32	4	32	83.3, 100, 100

Continued

TABLE 1—Continued

Organism (no. of strains) and antibiotic	MIC (μg/ml) <sup>a</sup>			% Susceptible <sup>b</sup>
	Range	50%	90%	
Amoxicillin-clavulanate	2–8	2	8	77.8, 100
Cefoxitin	16–128	16	32	50, 94
Cefotetan	64–>128	64	128	0, 0
Clindamycin	0.5–>128	4	>128	38.9, 72.2
Metronidazole	1–2	2	2	100, 100
<i>Bacteroides distasonis</i> (18)				
Trovafoxacin	0.06–0.25	0.125	0.25	100, 100, 100
Levofloxacin	0.5–4	2	4	77.8, 100
Ofloxacin	2–16	4	16	27.8, 72.7
Ciprofloxacin	8–>32	16	>32	0, 0
Imipenem	0.25–4	0.5	1	100, 100
Piperacillin-tazobactam	8–>128	64	>128	22.2, 33.3, 88.9
Amoxicillin-clavulanate	≤0.5–16	4	8	55.6 88.9
Cefoxitin	16–64	32	64	16.7, 72.2
Cefotetan	4–>128	128	>128	5.6, 5.6
Clindamycin	≤0.5–>128	4	8	44.4, 50
Metronidazole	≤0.5–2	≤0.5	2	100, 100
<i>Bacteroides vulgatus</i> (15)				
Trovafoxacin	0.06–0.125	0.06	0.125	100, 100, 100
Levofloxacin	2–4	2	4	85.7, 100
Ofloxacin	4–8	8	8	0, 6.7
Ciprofloxacin	16–>32	>32	>32	0, 0
Imipenem	≤0.125–1	0.25	1	100, 100
Piperacillin-tazobactam	1–32	4	16	93.3, 100, 100
Amoxicillin-clavulanate	≤0.5–8	≤0.5	1	93.3, 100
Cefoxitin	4–32	8	32	86.7, 100
Cefotetan	4–128	4	128	73.3, 73.3
Clindamycin	≤0.5–>128	≤0.5	>128	60, 60
Metronidazole	≤0.5–1	≤0.5	1	100, 100
<i>Bacteroides uniformis</i> (15)				
Trovafoxacin	0.06–0.5	0.125	0.5	100, 100, 100
Levofloxacin	2–16	2	4	66.7, 93.3
Ofloxacin	4–32	8	8	0, 6.7
Ciprofloxacin	8–32	16	32	0, 0
Imipenem	≤0.125–0.5	0.25	0.5	100, 100
Piperacillin-tazobactam	≤0.5–16	2	16	100, 100, 100
Amoxicillin-clavulanate	≤0.5–1	≤0.5	≤0.5	100, 100
Cefoxitin	2–32	8	32	60, 100
Cefotetan	4–128	32	128	26.7, 60
Clindamycin	≤0.5–>128	2	>128	53.3, 66.7
Metronidazole	≤0.5–2	1	2	100, 100
<i>Bacteroides caccae</i> (13)				
Trovafoxacin	0.06–1	0.5	1	100, 100, 100
Levofloxacin	2–8	4	4	15.4, 92.3
Ofloxacin	4–16	8	16	0, 15.4
Ciprofloxacin	8–16	8	16	0, 0
Imipenem	≤0.125–1	0.25	0.5	100, 100
Piperacillin-tazobactam	2–32	4	32	61.5, 100, 100
Amoxicillin-clavulanate	≤0.5–1	≤0.5	1	100, 100
Cefoxitin	2–32	16	32	84.6, 100
Cefotetan	8–>128	64	128	30.7, 38.5
Clindamycin	≤0.5–>128	2	8	76.9, 92.3
Metronidazole	≤0.5–4	≤0.5	2	100, 100

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TABLE 1—Continued

Organism (no. of strains) and antibiotic	MIC (μg/ml) <sup>a</sup>			% Susceptible <sup>b</sup>
	Range	50%	90%	
<i>Bacteroides merdae</i> / <i>Bacteroides stercoris</i> group (13) <sup>k</sup>				
Trovaflaxacin	≤0.015–1	0.5	1	100, 100, 100
Levofloxacin	1–4	1	2	76.9, 100
Ofloxacin	2–8	4	8	30.7, 69.2
Ciprofloxacin	1–16	4	16	7.6, 30.7
Imipenem	≤0.125–4	≤0.125	1	100, 100
Piperacillin- tazobactam	1–>128	4	16	91.6, 91.6, 91.6
Amoxicillin- clavulanate	≤0.5–2	≤0.5	≤0.5	100, 100
Cefoxitin	1–32	4	32	69.2, 100
Cefotetan	2–>128	8	>128	53.8, 53.8
Clindamycin	≤0.5–>128	1	>128	76.9, 76.9
Metronidazole	≤0.5–4	≤0.5	1	100, 100
<i>Prevotella</i> spp., <i>Porphy-</i> <i>romonas</i> spp., and other gram-negative spp. (13) <sup>l</sup>				
Trovaflaxacin	≤0.015–0.5	0.125	0.5	100, 100, 100
Levofloxacin	0.125–8	0.5	8	84.6, 84.6
Ofloxacin	0.125–16	2	16	76.9, 84.6
Ciprofloxacin	0.03–32	1	32	76.9, 76.9
Imipenem	≤0.125–1	≤0.125	0.5	100, 100
Piperacillin- tazobactam	≤0.5–4	≤0.5	4	100, 100, 100
Amoxicillin- clavulanate	≤0.5	≤0.5	≤0.5	100, 100
Cefoxitin	≤0.25–8	≤0.25	2	100, 100
Cefotetan	≤0.25–128	1	8	92.3, 92.3
Clindamycin	≤0.5–≤0.5	≤0.5	≤0.5	100, 100
Metronidazole	≤0.5–1	≤0.5	1	100, 100
<i>Fusobacterium</i> spp. (11) <sup>m</sup>				
Trovaflaxacin	≤0.015–4	0.25	2	63.6, 90.9, 100
Levofloxacin	≤0.015–4	0.25	4	72.7, 100
Ofloxacin	≤0.015–8	0.5	8	72.7, 72.7
Ciprofloxacin	≤0.015–8	0.25	4	63.6, 72.7
Imipenem	≤0.125–1	≤0.125	0.5	100, 100
Piperacillin- tazobactam	≤0.5–4	≤0.5	2	100, 100, 100
Amoxicillin- clavulanate	≤0.5–2	≤0.5	1	100, 100
Cefoxitin	≤0.25–8	1	4	100, 100
Cefotetan	≤0.25–4	0.5	4	100, 100
Clindamycin	≤0.5–8	0.5	4	81.4, 90.9
Metronidazole	≤0.5	≤0.5	≤0.5	100, 100
<i>Bacteroides gracilis</i> (10)				
Trovaflaxacin	0.06–0.5	0.125	0.25	100, 100, 100
Levofloxacin	0.06–0.5	0.06	0.5	100, 100
Ofloxacin	0.25–1	0.25	0.5	100, 100
Ciprofloxacin	0.06–0.5	0.125	0.5	100, 100
Imipenem	≤0.125–0.5	≤0.125	0.25	100, 100
Piperacillin- tazobactam	64–>128	128	>128	0, 0, 30
Amoxicillin- clavulanate	≤0.5–2	1	2	100, 100
Cefoxitin	≤0.5–16	1	4	100, 100
Cefotetan	1–4	4	4	100, 100
Clindamycin	≤0.5	≤0.5	≤0.5	100, 100
Metronidazole	≤0.5	≤0.5	≤0.5	100, 100
<i>Bilophila wadsworthia</i> (12)				
Trovaflaxacin	≤0.015–0.25	≤0.015	0.25	100, 100, 100

Continued

TABLE 1—Continued

Organism (no. of strains) and antibiotic	MIC ( $\mu\text{g/ml}$ ) <sup>a</sup>			% Susceptible <sup>b</sup>
	Range	50%	90%	
Ciprofloxacin	0.03–0.25	0.125	0.25	100, 100
Imipenem	≤0.125–1	≤0.125	≤0.125	100, 100
Piperacillin- tazobactam	≤0.5–8	≤0.5	8	100, 100, 100
Amoxicillin- clavulanate	≤0.5	≤0.5	≤0.5	100, 100
Cefoxitin	≤0.25–4	0.5	4	100, 100
Cefotetan	≤0.25–8	0.5	1	100, 100
Clindamycin	≤0.5	≤0.5	≤0.5	100, 100
Metronidazole	≤0.5	≤0.5	≤0.5	100, 100
<i>Clostridium</i> spp. (11) <sup>n</sup>				
Trovaflaxacin	≤0.015–0.125	0.06	0.125	100, 100, 100
Levofloxacin	0.5–4	0.5	2	90.9, 100
Ofloxacin	1–16	2	4	54.5, 81.8
Ciprofloxacin	0.5–8	1	4	54.5, 81.8
Imipenem	≤0.125–1	≤0.125	≤0.125	100, 100
Piperacillin- tazobactam	≤0.5	≤0.5	≤0.5	100, 100, 100
Amoxicillin- clavulanate	≤0.5	≤0.5	≤0.5	100, 100
Cefoxitin	0.5–64	2	16	90.9, 90.9
Cefotetan	≤0.25–128	1	32	81.8, 90.9
Clindamycin	0.5–4	1	4	81.8, 100
Metronidazole	≤0.5–4	≤0.5	2	100, 100
<i>Peptostreptococcus</i> spp. (12) <sup>o</sup>				
Trovaflaxacin	≤0.015–0.25	≤0.015	0.125	100, 100, 100
Levofloxacin	≤0.015–0.25	0.06	0.25	100, 100
Ofloxacin	≤0.015–0.5	0.25	0.5	100, 100
Ciprofloxacin	≤0.015–1	0.25	0.25	100, 100
Imipenem	≤0.125	≤0.125	≤0.125	100, 100
Piperacillin- tazobactam	≤0.5	≤0.5	≤0.5	100, 100, 100
Amoxicillin- clavulanate	≤0.5	≤0.5	≤0.5	100, 100
Cefoxitin	≤0.5	≤0.5	≤0.5	100, 100
Cefotetan	≤0.5	≤0.5	≤0.5	100, 100
Clindamycin	≤0.5	≤0.5	≤0.5	100, 100
Metronidazole	≤0.5–128	≤0.5	64	66.7, 75
Non-spore-forming gram-positive bacilli (17) <sup>p</sup>				
Trovaflaxacin	≤0.015–1	0.125	1	100, 100, 100
Levofloxacin	≤0.015–0.25	≤0.015	0.25	100, 100
Ofloxacin	≤0.015–0.5	0.03	0.5	100, 100
Levofloxacin	≤0.015–4	0.125	2	94.1, 100
Ofloxacin	0.125–16	0.5	8	76.5, 88.2
Ciprofloxacin	0.06–>32	0.5	4	76.5, 82.3
Imipenem	≤0.125–0.5	≤0.125	0.5	100, 100
Piperacillin- tazobactam	≤0.5–16	4	16	100, 100, 100
Amoxicillin- clavulanate	≤0.5	≤0.5	≤0.5	100, 100
Cefoxitin	≤0.5–32	4	16	94.1, 100
Cefotetan	1–64	16	32	70.6, 94.1
Clindamycin	≤0.5–4	≤0.5	4	88.2, 100
Metronidazole	≤0.5–>128	≤0.5	>128	70.6, 70.6

<sup>a</sup> 50% and 90%, MICs at which 50 and 90% of the isolates are inhibited, respectively.

<sup>b</sup> Interpretive breakpoints for trovaflaxacin have not been approved yet by the National Committee for Clinical Laboratory Standards. Percent susceptible at the following concentrations: for trovaflaxacin, 1, 2, and 4  $\mu\text{g/ml}$ ; for levofloxacin and ofloxacin, 2 and 4  $\mu\text{g/ml}$ ; for ciprofloxacin, 1 and 2  $\mu\text{g/ml}$ ; for imipenem, 4 and 8  $\mu\text{g/ml}$ ; for piperacillin-tazobactam, 16, 32, and 64  $\mu\text{g/ml}$ ; for amoxicillin-clavulanate, 8 and 16  $\mu\text{g/ml}$ ; for cefoxitin, 8 and 16  $\mu\text{g/ml}$  for facultative organ-

TABLE 1—Continued

isms and 16 and 32 µg/ml for anaerobes; for cefotetan, 16 and 32 µg/ml; for gentamicin, 4 and 8 µg/ml; for clindamycin, 2 and 4 µg/ml; for metronidazole, 8 and 16 µg/ml.

- <sup>c</sup> *K. pneumoniae*, *n* = 8; *K. oxytoca*, *n* = 7; *K. ozaenae*, *n* = 5.  
<sup>d</sup> *C. freundii*, *n* = 16; *C. amalonaticus*, *n* = 2; *Citrobacter* spp. *n* = 3.  
<sup>e</sup> *E. aerogenes*, *n* = 4; *E. cloacae*, *n* = 6.  
<sup>f</sup> *M. morgani*, *n* = 9; *P. stuartii*, *n* = 6; *P. rettgeri*, *n* = 1.  
<sup>g</sup> *P. mirabilis*, *n* = 10; *P. vulgaris*, *n* = 1.  
<sup>h</sup> *E. faecalis*, *n* = 11; *E. faecium*, *n* = 6; *E. avium*, *n* = 10; *E. durans*, *n* = 1; *E. casseliflavus*, *n* = 1.  
<sup>i</sup> *S. milleri* group, *n* = 24; *S. cremoris*, *n* = 2; *S. salivarius*, *n* = 1; *S. mitis*, *n* = 1; *S. lactis*, *n* = 1.  
<sup>j</sup> *S. epidermidis*, *n* = 14; *S. aureus*, *n* = 1; *S. haemolyticus*, *n* = 3; *S. warneri*, *n* = 2; *S. xylosus*, *n* = 2; *S. simulans*, *n* = 1; *S. capitis*, *n* = 1.  
<sup>k</sup> *B. merdae*, *n* = 8; *B. stercoris*, *n* = 5.  
<sup>l</sup> *Prevotella bivia*, *n* = 2; *Prevotella buccae*, *n* = 2; *Prevotella intermedia*, *n* = 2; *Prevotella oralis*, *n* = 1; *Porphyromonas asaccharolytica*, *n* = 1; *Porphyromonas levii*, *n* = 1; *Bacteroides* sp., *n* = 2; *Desulfomonas* sp., *n* = 2.  
<sup>m</sup> *F. varium*, *n* = 4; *F. mortiferum*, *n* = 1; *F. nucleatum*, *n* = 1; *Fusobacterium* sp., *n* = 5.  
<sup>n</sup> *C. perfringens*, *n* = 6; *C. ramosum*, *n* = 1; *C. clostridioforme*, *n* = 1; *C. parvutrophicum*, *n* = 1; *C. subterminale*, *n* = 1; *C. hastiforme*, *n* = 1.  
<sup>o</sup> *P. micros*, *n* = 6; *P. anaerobius*, *n* = 5; *P. prevotii*, *n* = 1.  
<sup>p</sup> *Eubacterium lentum*, *n* = 8; *Eubacterium* sp., *n* = 3; *Propionibacterium* sp., *n* = 3; *Actinomyces* sp., *n* = 3.

collin-clavulanate against all of the anaerobes tested. Trovafloxacin had good activities against members of the *B. fragilis* group species other than *B. fragilis*, in contrast to clindamycin, cefoxitin, and cefotetan, which had poor activities against these strains. Piperacillin-tazobactam was active against 96.2% of the isolates of the *B. fragilis* group at the breakpoint concentration of 64 µg/ml. Levofloxacin was the only other quinolone in this study that was moderately active against the *B. fragilis* group. Overall, trovafloxacin inhibited 99.3% of the intra-abdominal isolates tested at a concentration of 2 µg/ml.

Our results for trovafloxacin are comparable to data published by other investigators. Spangler et al. (9) and Wexler et al. (11) reported that >96% of the anaerobes they tested were susceptible to trovafloxacin at ≤2 mg/ml. Gooding and Jones (4), Girard et al. (2), and Eliopoulos et al. (1a) reported similar good activities against gram-positive species, as well as against *Enterobacteriaceae* and *P. aeruginosa*. Trovafloxacin has a spectrum of activity similar to that of clinafloxacin and is more active against anaerobes and gram-positive species than temafloxacin, an older fluoroquinolone that has been withdrawn from the market (1a, 3).

Trovafloxacin has excellent in vitro activities against diverse bacteria isolated from intra-abdominal infections. It has po-

tential use as a single agent for treatment of polymicrobial infections.

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